

IN THE CLAIMS:

Please cancel claims 1-37 without prejudice.

Insert the following new claims.

38. A method of detecting and/or quantifying an antibody in a liquid sample comprising the steps of:

(o') providing a mixture of a liquid phase and a two-component solid phase complex composed of (i) the antibody of the sample, and (ii) a reactant antibody directed against the sample antibody, the reactant antibody being bound to a solid particle;

(p') separating the two-component solid phase complex from the liquid phase;

(q') washing the separated two-component solid phase complex to remove non-complex bound compounds;

(r') adding to the washed two-component solid phase complex a solution of (iii) a ligand in the form of an antigen, an antibody or a hapten, which is optionally labeled, to form a three-compound solid phase complex;

(s') optionally adding to the three-component solid phase complex a solution of (iv) a label compound to form a four-component solid phase complex;

(t') separating the three- or four-component solid phase complex obtained in step (r') or (s'), respectively, from the solution;

(u') washing the separated multi-component solid phase complex to remove non-complex bound compounds; and

(v') performing a detection/measurement of the washed labeled multi-component complex.

39. A method of detecting and/or quantifying an antibody in a liquid sample comprising the steps of:

(o) providing a mixture of a liquid phase and a two-component solid phase complex composed of (i) the antibody of the sample, and (ii) a reactant antibody

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directed against the sample antibody, the reactant antibody being bound to a solid particle;

- (p) separating the two-component solid phase complex from the liquid phase;
- (q) washing the separated two-component, solid phase complex to remove non-complex bound compounds;
- (r) adding to the washed two-component solid phase complex a solution of (iii) a ligand in the form of an antigen, an antibody or a hapten, which is bound to biotin or a functional derivative thereof, to form a three-component solid phase complex;
- (s) adding to the three-component solid phase complex a solution of (iv) a chemiluminescent compound covalently bound to avidin, streptavidin or a functional derivative thereof to form a four-component solid phase complex;
- (t) separating the four-component solid phase complex from the solution;
- (u) washing the separated four-component solid phase complex to remove non-complex bound compound (iv); and
- (v) initiating a chemiluminescent reaction in the washed four-component solid phase complex and detecting/measuring the resulting chemiluminescence, if any.

40. A method of detecting and/or quantifying an antibody in a liquid sample comprising the steps of:

(o'') providing a mixture of a liquid phase and a two-component solid phase complex composed of (i) the antibody of the sample, and (ii) a reactant antibody directed against the sample antibody, the reactant antibody being bound to a solid paramagnetic particle;

(p'') separating magnetically the two-component solid phase complex from the liquid phase;

(q'') washing the separated two-component solid phase complex to remove non-complex bound compounds;

(r'') adding to the washed two-component solid phase complex a solution of (iii) a ligand in the form of an antigen, an antibody or a hapten, which is bound to biotin or a functional derivative thereof, to form a three-component solid phase complex;

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(s'') adding to the three-component solid phase complex a solution of (iv) a chemiluminescent compound covalently bound to avidin, streptavidin or a functional derivative thereof to form a four-component solid phase complex;

5 (t'') separating magnetically the four-component solid phase complex from the solution;

(u'') washing the separated four-component solid phase complex to remove non-complex bound compound (iv); and

(v'') initiating a chemiluminescent reaction in the washed four-component solid phase complex and detecting/measuring the resulting chemiluminescence, if any.

10 41. A method according to claim 39, wherein the chemiluminescent compound is an acridinium compound.

42. A method according to claim 40, wherein the chemiluminescent compound is an acridinium compound.

15 43. A method according to claim 38, wherein component (iii) of step (r'), and component (iv) of step (s'), respectively, are added in one operation.

44. A method according to claim 39, wherein component (iii) of step (r) and component (iv) of step (s) respectively, are added in one operation.

20 45. A method according to claim 40, wherein component (iii) of step (r'') and component (iv) of step (s''), respectively, are added in one operation.

46. A method according to claim 39, wherein the three-component solid phase complex formed in step (r) prior to subjecting it to step(s) is washed to remove non-complex bound compounds.

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47. A method according to claim 40, wherein the three-component solid phase complex formed in step (r') prior to subjecting it to step (s'), is washed to remove non-complex bound compounds.

48. A method of evaluating and/or predicting the effect of a Specific Allergy Vaccination treatment comprising the steps of:

(h') determining the content of an antibody in a liquid sample using the following assay;

(a') providing a mixture of a liquid phase and a three-component solid phase complex composed of (i) the antibody of the sample, (ii) a reactant antibody directed against the sample antibody, the reactant antibody being bound to a solid particle, and (iii) a ligand in the form of an antigen, an antibody or a hapten,

(b') separating the three-component solid phase complex from the liquid phase,

(c') washing the separated three-component solid phase complex to remove non-complex bound compounds,

(d') adding to the three-component solid phase complex a solution of (iv) a label compound to form a four-component complex,

(e') separating the four-component solid phase complex from the solution,

(f') washing the separated four-component solid phase complex to remove non-complex bound compound (iv),

(g') performing a detection/measurement of the washed labeled four-component complex.

(i') determining the content of the said antibody using the following assay;

(ia') providing a mixture of a liquid phase and a four-component solid phase complex composed of (i) the antibody of the sample, (ii) a reactant antibody directed against the sample antibody, the reactant antibody being bound to a solid particle, (iii) a ligand in the form of an antigen, an antibody or a hapten, and (iv) a label compound, to form a four-component solid phase complex,

(ib') separating the four-component solid phase complex from the liquid phase,

(ic') washing the separated four-component solid phase to remove non-complex bound compounds, and

(id') performing a detection/measurement of the washed labeled four-component complex,

(j') comparing the measurements obtained in step (h') and step (i') and using the comparison to evaluate and/or predict the effect of the Specific Allergy Vaccination treatment.

49. A method of evaluating and/or predicting the effect of a Specific Allergy Vaccination treatment comprising the steps of:

(h) determining the content of an antibody in a liquid sample using the following assay;

(a) providing a mixture of a liquid phase and a three-component solid phase complex composed of (i) the antibody of the sample, (ii) a reactant antibody directed against the sample antibody, the reactant antibody being bound to a solid particle, and (iii) a ligand in the form of an antigen, and antibody or a hapten, which is bound to biotin or a functional derivative thereof,

(b) separating the three-component solid phase complex from the liquid phase,

(c) washing the separated three-component solid phase complex to remove non-complex bound compounds,

(d) adding to the three-component solid phase complex a solution of (iv) a chemiluminescent compound covalently bound to avidin, streptavidin or a functional derivative thereof to form a four-component solid phase complex,

(e) separating the four-component solid phase complex from the solution,

(f) washing the separated four-component solid phase complex to remove non-complex bound compound (iv), and

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(g) initiating a chemiluminescent reaction in the washed four-component solid phase complex and detecting/measuring the resulting chemiluminescence, if any,

(i) determining the content of the said antibody using the following assay;

(ia) providing a mixture of a liquid phase and a four-component solid phase complex composed of (i) the antibody of the sample, (ii) a reactant antibody directed against the sample antibody, the reactant antibody being bound to a solid particle, (iii) a ligand in the form of an antigen, an antibody or a hapten, which is bound to biotin or a functional derivative thereof, and (iv) a chemiluminescent compound covalently bound to avidin, streptavidin or a functional derivative thereof, to form a four-component solid phase complex,

(ib) separating the four-component solid phase complex from the liquid phase,

(ic) washing the separated four-component solid phase to remove non-complex bound compounds, and

(id) initiating a chemiluminescent reaction in the washed four-component solid phase complex and measuring the resulting chemiluminescent, if any, and

(j) comparing the measurements obtained in step (h) and step (i) and using the comparison to evaluate and/or predict the effect of the Specific Allergy Vaccination treatment.

50. A method of evaluating and/or predicting the effect of a Specific Allergy Vaccination treatment comprising the steps of:

(h'') determining the content of an antibody in a liquid sample using the following assay;

(a'') providing a mixture of a liquid phase and a three-component solid phase complex composed of (i) the antibody of the sample, (ii) a reactant antibody directed against the sample antibody, the reactant antibody being bound to a solid paramagnetic particle, and (iii) a ligand in the form of an antigen, an antibody or a hapten, which is bound to biotin or a functional derivative thereof,

(b'') separating magnetically the three-component solid phase complex from the liquid phase,

(c'') washing the separated three-component solid phase complex to remove non-complex bound compounds,

5 (d'') adding to the three-component solid phase complex a solution of (iv) a chemiluminescent compound covalently bound to avidin, streptavidin or a functional derivative thereof to form a four-component solid phase complex,

(e'') separating magnetically the four-component solid phase complex from the solution,

10 (f'') washing the separated four-component solid phase complex to remove non-complex bound compound (iv),

(g'') initiating a chemiluminescent reaction in the washed four-component solid phase complex and detecting/measuring the resulting chemiluminescence, if any,

15 (i'') determining the content of the said antibody using the following assay;

(ia'') providing a mixture of a liquid phase and a four-component solid phase complex composed of (i) the antibody of the sample, (ii) a reactant antibody directed against the sample antibody, the reactant antibody being bound to a solid paramagnetic particle, (iii) a ligand in the form of an antigen, an antibody or a hapten, 20 which is bound to biotin or a functional derivative thereof, and (iv) a chemiluminescent compound covalently bound to avidin, streptavidin or a functional derivative thereof, to form a four-component solid phase complex,

(ib'') separating magnetically the four-component solid phase complex from the liquid phase,

25 (ic'') washing the separated four-component solid phase to remove non-complex bound compounds,

(id'') initiating a chemiluminescent reaction in the washed four-component solid phase complex and measuring the resulting chemiluminescence, if any, and

(j'') comparing the measurements obtained in step (h'') and step (i'') and using the comparison to evaluate and/or predict the effect of the Specific Allergy Vaccination treatment.

51. A method of evaluating and/or predicting the effect of a Specific Allergy Vaccination treatment comprising the steps of:

(x') determining the content of an antibody in a liquid sample using the method of claim 38;

(y') determining the content of the said antibody using the following assay:

(ya') providing a mixture of a liquid phase and a three-component solid phase complex composed of (i) the antibody of the sample, (ii) a reactant antibody directed against the sample antibody, the reactant antibody being bound to a solid particle, (iii) a ligand in the form of an antigen, an antibody or a hapten which is labeled or bound to (iv) a label compound, to form a multi-component solid phase complex,

(yb') separating the multi-component solid phase complex from the liquid phase,

(yc') washing the separated multi-component solid phase to remove non-complex bound compounds, and

(yd') performing a detection/measurement of the washed labeled multi-component complex, and

(z') comparing the measurements obtained in step (x') and step (y') and using the comparison to evaluate and/or predict the effect of the Specific Allergy Vaccination treatment.

52. A method of evaluating and/or predicting the effect of a Specific Allergy Vaccination treatment comprising the steps of:

(x) determining the content of an antibody in a liquid sample using the method of claim 39, --

(y) determining the content of the said antibody using the following assay:

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(yb'') separating magnetically the four-component solid phase complex from the liquid phase,

(yc'') washing the separated four-component solid phase to remove non-complex bound compounds,

(yd') initiating a chemiluminescent reaction in the washed four-component solid phase complex and measuring the resulting chemiluminescent, if any, and

(z'') comparing the measurements obtained in step (x'') and step (y'') and using the comparison to evaluate and/or predict the effect of the Specific Allergy Vaccination treatment.

54. A method according to claim 48, wherein step (ia') is carried out by mixing components (i) and (ii), then adding component (iii), and finally adding component (iv), if added.

55. A method according to claim 49 wherein step (ia) is carried out by mixing components (i) and (ii), then adding component (iii), and finally adding component (iv), if added.

56. A method according to claim 50, wherein step (ia' ') is carried out by mixing components (i) and (ii), then adding component (iii), and finally adding component (iv), if added.

57. A method according to claim 51, wherein step (ya') is carried out by mixing components (i) and (ii), then adding component (iii), and finally adding component (iv), if added.

58. A method according to claim 52, wherein step (ya) is carried out by mixing components (i) and (ii), then adding component (iii), and finally adding component (iv), if added.

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59. A method according to claim 53 wherein step (ya' ') is carried out by mixing components (i) and (ii), then adding component (iii), and finally adding component (iv), if added.

5 60. A method according to claim 48, wherein step (ia'), is carried out by mixing components (i), (ii) and (iii), and then adding component (iv), if added.

61. A method according to claim 49, wherein step (ia), is carried out by mixing components (i), (ii) and (iii), and then adding component (iv), if added.

62. A method according to claim 50, wherein step (ia' '), is carried out by mixing components (i), (ii) and (iii), and then adding component (iv), if added.

10 63. A method according to claim 51, wherein step (ya') is carried out by mixing components (i), (ii) and (iii), and then adding component (iv), if added.

64. A method according to claim 52, wherein step(ya) is carried out by mixing components (i), (ii) and (iii), and then adding component (iv), if added.

15 65. A method according to claim 53, wherein step (ya' '), is carried out by mixing components (i), (ii) and (iii), and then adding component (iv), if added.

66. A method according to claim 48, wherein the comparison of step (j') is carried out by calculating the ratio of the measurements obtained in the two said steps.

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67. A method according to claim 49, wherein the comparison of step (j) is carried out by calculating the ratio of the measurements obtained in the two said steps.

20 68. A method according to claim 50, wherein the comparison of step (j' ') is carried out by calculating the ratio of the measurements obtained in the two said steps.

69. A method according to claim 51, wherein the comparison of step (z') is carried out by calculating the ratio of the measurements obtained in the two said steps.

70. A method according to claim 52, wherein the comparison of step (z) is carried out by calculating the ratio of the measurements obtained in the two said steps.

5 71. A method according to claim 53, wherein the comparison of step (z'') is carried out by calculating the ratio of the measurements obtained in the two said steps.

10 72. A method according to claim 48, wherein the comparison of step (j') is carried out at a number of points in time at the start of and during the treatment period, and that any temporal change, which may be observed, is used as a basis for evaluating and/or predicting the effect of the treatment.

73. A method according to claim 49, wherein the comparison of step (j) is carried out at a number of points in time at the start of and during the treatment period, and that any temporal change, which may be observed, is used as a basis for evaluating and/or predicting the effect of the treatment.

15 74. A method according to claim 50, wherein the comparison of step (j'') is carried out at a number of points in time at the start of and during the treatment period, and that any temporal change, which may be observed, is used as a basis for evaluating and/or predicting the effect of the treatment.

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20 75. A method according to claim 51, wherein the comparison of step (z') is carried out at a number of points in time at the start of and during the treatment period, and that any temporal change, which may be observed, is used as a basis for evaluating and/or predicting the effect of the treatment.

76. A method according to claim 52, wherein the comparison of step (z) is carried out at a number of points in time at the start of and during the treatment period,

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and that any temporal change, which may be observed, is used as a basis for evaluating and/or predicting the effect of the treatment.

5 77. A method according to claim 53, wherein the comparison of step (z') is carried out at a number of points in time at the start of and during the treatment period, and that any temporal change, which may be observed, is used as a basis for evaluating and/or predicting the effect of the treatment.

78. A method according to claim 38, wherein the label compound is selected from the group consisting of a luminescent label, a chemiluminescent label, an enzyme label, a radioactivity label, a fluorescent label and an absorbance label.

10 79. A method according to claim 38, wherein the labeled ligand is labeled by a radioactive atom.

15 80. A method according to claim 38, wherein the separation of the solid phase complex from the liquid phase is carried out by a member selected from the group consisting of magnetic separation, filtration, sedimentation, centrifugation, chromatography and column chromatography.

81. A method of evaluating the immunological status of a subject comprising the steps of:

20 1) determining the content of an antibody in a liquid sample from the subject using an immunoassay, wherein the reaction between the antibody of the sample and a ligand in the form of an antigen, an antibody or a hapten, the ligand being directed to the Fab region of the sample antibody, is carried out in the presence of other constituents of the sample to obtain a first measurement,

25 2) determining the content of an antibody in the liquid sample using an immunoassay, wherein the reaction between the antibody of the sample and a ligand in the form of an antigen, an antibody or a hapten, the ligand being directed to the Fab

region of the sample antibody, is carried out in the absence of other constituents of the sample to obtain a second measurement, and

3) interrelating the first and second measurements to express an interference and using the interference as a parameter for evaluating the immunological status of the subject.

82. A method of evaluating the immunological status of a subject comprising the steps of:

A) determining the content of an antibody in a liquid sample from the subject using the following assay protocol (assay A);

(Aa) mixing (i) the antibody of the sample, (ii) an antibody directed against the Fc region of the sample antibody, the reactant antibody being bound to a solid carrier and (iii) a ligand in the form of an antigen, an antibody or a hapten, the ligand being directed to the Fab region of the sample antibody, to form a mixture of a three-component solid phase complex and a liquid phase,

(Ab) contacting the three-component complex with (iv) a label compound to form a mixture of a four-component complex and a liquid phase,

(Ac) washing the four-component solid phase to remove non-complex bound compounds,

(Ad) performing a detection/measurement of the washed labeled four-component complex to obtain a measurement A;

(B) determining the content of the said antibody in the said sample using the following assay protocol (assay B):

(Ba) mixing (i) the antibody of the sample, and (ii) a reactant antibody directed against the Fc region of the sample antibody, the reactant being bound to a solid carrier, to form a mixture of a two-component solid phase complex and a liquid phase,

(Bb) washing the two-component solid phase complex to remove non-complex bound compounds,

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(Bc) contacting the washed two-component solid phase complex with a (iii) a ligand in the form of an antigen, an antibody or a hapten, the ligand being bound to the Fab region of the sample antibody, and (iv) a label compound, to form a mixture of a four-component solid phase complex and a liquid phase,

(Bd) washing the four-component solid phase complex to remove non-complex bound compounds,

(Be) performing a detection/measurement of the washed labeled four-component complex to obtain a measurement B; and

(E) interrelating measurements A and B to express an interference and using the interference as a parameter for evaluating the immunological status of the subject.

83. A method according to claim 82, wherein the label compound is a luminescent label, a chemiluminescent label, an enzyme label, a radioactive label, a fluorescent label or an absorbance label.

84. A method according to claim 82, wherein the (iii) ligand is biotinylated.

85. A method according to claim 84, wherein the (iv) label compound is a chemiluminescent compound covalently bound to avidin, streptavidin or a functional derivative thereof.

86. A method according to claim 81, wherein the subject to be evaluated is undergoing allergy treatment, allergy vaccination treatment or Specific Allergy Vaccination (SAV) treatment.

87. A method according to claim 82, wherein the subject to be evaluated is undergoing allergy treatment, allergy vaccination treatment or Specific Allergy Vaccination (SAV) treatment.

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88. A method of evaluating the effect of allergy treatment of a subject comprising the steps of:

A) determining the content of the said antibody using the following assay protocol (assay A);

(Aa) mixing (i) the antibody of the sample, (ii) an antibody directed against the Fc region of the sample antibody, the reactant antibody being bound to a solid carrier and (iii) a ligand in the form of an antigen, an antibody or a hapten, the ligand being directed to the Fab region of the sample antibody, to form a mixture of a three-component solid phase complex and a liquid phase,

(Ab) contacting the three-component complex with (iv) a label compound to form a mixture of a four-component complex and a liquid phase,

(Ac) washing the four-component solid phase to remove non-complex bound compounds,

(Ad) performing a detection/measurement of the washed labeled four-component complex to obtain a measurement A;

(E) using measurement A as a parameter for evaluating the effect of the treatment.

89. A method of evaluating the effect of allergy treatment of a subject comprising the steps of:

(C) determining the content of the said antibody using the following assay protocol (assay C);

(Ca) mixing (i) the antibody of the sample, (ii) an antibody directed against the Fc region of the sample antibody, the reactant antibody being bound to a solid carrier and (iii) a labeled ligand in the form of an antigen, an antibody or a hapten, the ligand being directed to the Fab region of the sample antibody, to form a mixture of three-component solid phase complex and a liquid phase,

(Cb) washing the three-component solid phase to remove non-complex bound compounds,

(Cc) performing a detection/measurement of the washed labeled four-component complex to obtain a measurement C, and

(E) using measurement C as a parameter for evaluating the effect of the treatment.

5 90. A method according to claim 88, wherein the subject to be evaluated is undergoing allergy vaccination treatment or Specific Allergy Vaccination (SAV) treatment.

10 91. A method according to claim 89, wherein the subject to be evaluated is undergoing allergy vaccination treatment or Specific Allergy Vaccination (SAV) treatment.

 92. A method according to claim 88, wherein the evaluation in step E) is carried out at a number of points in time at the start of and during the treatment period, and that any temporal change, which may be observed, is used as a basis for evaluating and/or predicting the effect of the treatment.

15 93. A method according to claim 89, wherein the evaluation in step E) is carried out at a number of points in time at the start of and during the treatment period, and that any temporal change, which may be observed, is used as a basis for evaluating and/or predicting the effect of the treatment.

 94. A method according to claim 82, wherein the carrier is a particle.

20 95. A method according to claim 81, wherein the sample antibody is a specific IgE.

 96. A method according to claim 82, wherein the sample antibody is a specific IgE.

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97. A method according to claim 88, wherein the sample antibody is a specific IgE.

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98. A method according to claim 89, wherein the sample antibody is a specific IgE.
